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USSN: 10/527,771

Attorney Docket: 1-2002.015 US

Response to Office Action of March 27, 2006

Amendments to the Specification

Please replace the paragraph at page 4, lines 22-28 with the following paragraph:

The level of nucleotide homology can be determined with the computer program "BLAST 2 SEQUENCES" by selecting sub-program: "BLASTN" that can be found at the U.S. Department of Health and Human Services' National Institutes of Health's National Library of Medicine's National Center for Biotechnology Information internet site www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html. A reference for this program is Tatiana A. Talusova, Thomas L. Madden, FEMS Microbiol. Letters 174, 247-250 (1999). Parameters used are the default parameters: Reward for a match: +1. Penalty for a mismatch: -2. Open gap: 5. Extension gap: 2. Gap x_dropoff: 50.

Please replace the paragraph at page 10, lines 4-27 with the following paragraph:

A very attractive expression system for heterologous nematode gene expression is a nematodal expression system based upon the worm *Caenorhabditis elegans*. A heterologous expression system for this nematode has been described by Redmond, D. L. et al., in *Molecular and Biochemical Parasitology* 112,125-131 (2001). See also Hashmi, S. et al., in *Trends in Parasitology* 17, 387-393 (2001). The genes according to the present invention can be fused immediately downstream of a *C. elegans* cysteine protease promoter, *cpr-5*, which has been shown recently to direct expression to the gut of *C. elegans* (Redmond et al., 2001) and cloned into the pGEX-vector. The slow growing DR96 *unc76(e911)* *C. elegans* mutant strain can be transformed by micro-injection of plasmid DNA into the distal arm of the hermaphrodite gonad. The plasmid DNA can e.g. be prepared using the Qiagen method. *Ostertagia* genes according to the invention can be co-injected with the repair plasmid p76-16B. The p76-16B plasmid rescues the *unc76* phenotype and allows transformants to be identified through reversion back to the wild type phenotype. Transformed lines in which the second and subsequent generations show the wild

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type phenotype will be maintained. The presence of the injected construct in transgenic worms can easily be verified by PCR analysis of single worms with primers developed specifically for the DNA of interest (Kwa et al., Journal of Molecular Biology 246, 500-510. (1995)). Transgenic worms, rescued by p76-16B, grow more quickly than the unc76(e911) mutants and allow rapid accumulation of transgenic worm material. Because of its rapid life-cycle, transformants can be grown in vitro in large quantities. Somatic extracts of transgenic worms can be prepared by grinding the nematodes in a mortar under liquid nitrogen and resuspending them in 0.05M PBS containing 2% TRITONX-100® non-ionic detergent ~~TritonX-100®~~. Fusion proteins will be purified by affinity chromatography using a Glutathione Sepharose column.

Please replace the paragraph at page 14, line 34 to page 15, line 3 with the following paragraph:

The level of protein homology can be determined with the computer program "BLAST 2 SEQUENCES" by selecting sub-program: "BLASTP", that can be found at the U.S. Department of Health and Human Services' National Institutes of Health's National Library of Medicine's National Center for Biotechnology Information internet site ~~www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html~~. A reference for this program is Tatiana A. Tatusova, Thomas L. Madden, FEMS Microbiol. Letters 174, 247-250 (1999). Matrix used: "blosum62". Parameters used are the default parameters: Open gap: 11. Extension gap: 1. Gap x_dropoff: 50).

Please replace the paragraph on page 18, lines 14-28 with the following paragraph:

Methods for large-scale production of antibodies according to the invention are also known in the art. Such methods rely on the cloning of (fragments of) the genetic information encoding the

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protein according to the invention in a filamentous phage for phage display. Such techniques are described i.a. ~~at the "Antibody Engineering Page" under "filamentous phage display" at <http://aximf1.imt.uni-marburg.de/about.rek/aepphage.html>~~, and in review papers by Cortese, R. et al., (1994) in Trends in Biotechn. 12, 262-267, by Clackson, T. & Wells, J. A. (1994) in Trends in Biotechn. 12, 173-183, by Marks, J. D. et al., (1992) in J. Biol. Chem. 267, 16007-16010, by Winter, G. et al., (1994) in Annu. Rev. Immunol. 12, 433-455, and by Little, M. et al., (1994) Biotechn. Adv. 12, 539-555. The phages are subsequently used to screen camelid expression libraries expressing camelid heavy chain antibodies. (Muyldermans, S. and Lauwereys, M., Journ. Molec. Recogn. 12,131-140 (1999) and Ghahroudi, M. A. et al., FEBS Letters 414, 512-526 (1997)). Cells from the library that express the desired antibodies can be replicated and subsequently be used for large-scale expression of antibodies.

Please replace the paragraph on page 39, lines 4-15 with the following paragraph:

The coding regions for the 65, 28, 31, and 24 kD proteins of the invention were subcloned from their respective vectors into a pFastBac® plasmid (Invitrogen) using standard techniques. These FastBac constructs were transfected into Sf9 insect cells, to produce recombinant baculoviruses, according to the manufacturer's instructions (Invitrogen). Next expression cultures were run, using Sf9 and Sf158 insect cells, which were cultured in microcarrier spinner flasks of 100 and 250 ml. Serum free culture media used were CCM3™ (Hyclone), and SF900-II™ (Invitrogen). Cells were infected at an m.o.i. of 0.1-0.5 and cultured for 34 days. Then cultures were centrifuged, culture supernatant was harvested, and cell pellets were resuspended 10 x concentrated in PBS. TRITONX-100® non-ionic detergent ~~TritonX-100®~~ was added to all samples to a concentration of 0.2% v/v. Samples were extracted overnight at room temperature, centrifuged, and supernatants were stored at -20°C. until use.